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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/516,315

01/30/2006

Kimiko Murofushi

P26378

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7055 7590 07/15/2008
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EXAMINER

SHIAO, REI TSANG

ART UNIT

PAPER NUMBER

1626

NOTIFICATION DATE

DELIVERY MODE

07/15/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No. 10/516,315	Applicant(s) MUROFUSHI ET AL.	
	Examiner REI-TSANG SHIAO	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5 is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/02/07</u> . | 6) <input type="checkbox"/> Other: _____ |

This application supersedes the previous Office action dated 06/06/2008

DETAILED ACTION

1. This application claims benefit of the foreign application:
JAPAN 2002-169743 with a filing date 06/11/2002. However, an English-translated version of the instant foreign priority has not been filed to the Office, therefore the foreign priority has not been granted.
2. Claims 1-8 are pending in the application.

Information Disclosure Statement

3. Applicant's Information Disclosure Statement, filed on February 02, 2007 has been considered. Please refer to Applicant's copy of the 1449 submitted herein.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using compounds of formula (I) for treating cells *in vitro*, it does not reasonably provide enablement for using compounds of the formula (I) for treating cancer, *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining

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whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claims 7-8 is drawn to compositions with intent methods of use using compounds of formula (I) for treating cancer *in vitro* or *in vivo*.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in

the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Van Corven et al. publication, Cell, 1989, 59:45-54, disclose lysophosphatidate-induced cell proliferation, *in vitro*. Applicants are claiming compositions with intent methods of use using compounds of formula (I) effective to "treating cancer" *in vivo*. As such, the specification fails to enable the skilled artisan to use the compounds of claims 7-8 effective to "treating cancer" *in vivo*.

In addition, there is no established correlation between *in vitro* activity and accomplishing treatment of "treating cancer", *in vivo*, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use the compounds of the formula (I) since there is no description of an actual method wherein "treating cancer" *in vivo* in a host is treated.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compounds of claims 7-8 due to the unpredictability of the "treating cancer" *in vivo*. The "treating cancer" *in vivo* is known to have many obstacles that

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would prevent one of ordinary skill in the art from accepting treating or preventing regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of exemplary *in vitro* invasion assays of cells, *in vitro*, see pages 24-25 of the specification. There are no *in vivo* working examples present for the treatment cancer ameliorated by the administration of compounds of the instant invention.

The breadth of the claims

The breadth of the claims is compositions with intent methods of use of the instant compounds effective to “treating cancer” *in vivo*.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what “treating cancer” *in vivo* would be benefited (i.e., treated) by the administration of the instant compounds of the instant invention and would furthermore then have to determine which of the claimed methods of use would provide treatment of cancer *in vivo*, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be

individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which methods of use exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the pharmaceutical compounds of the instant claims 7-8 for the "treating cancer" *in vivo*. As a result necessitating one of skill to perform an exhaustive search for which "treating cancer" *in vivo*, can be treated by what pharmaceutical compounds of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. This rejection can be overcome by deletion of the preamble "which is used as an anticancer agent" or "which suppresses cancer cell invasion, so as to suppress metastasis of the cancer" would obviate the rejection.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5.1 Claims 1-2 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by

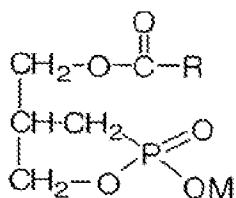
(1) Kawai et al. publication, Synthesis and Physiological Effects of Cyclic

Lysophosphatidic Acid and Carba-Derivative, "The 23rd symposium on Progression

Organic Reactions in Life Science," November 17 and 18 1997, The Pharmaceutical

Society of Japan, pp. 1-9; or (2) Liliom et al. CAS: 125:265929.

Applicants claim compounds/compositions of formula (I), i.e.,



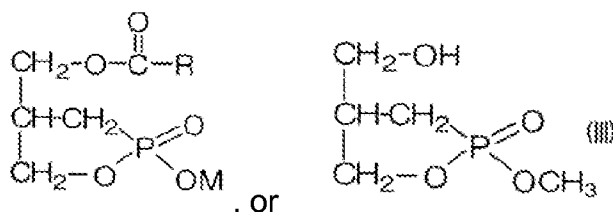
, wherein the variable M represents hydrogen or counter ion (i.e., Na), and the variable R represents alkyl, alkenyl or alkynyl, see claim 1.

Kawai et al. disclose a number of compounds, i.e., PHYLPA, No. 6a-6f, and compounds No. 13a, 13c, 13d, and 13f, see pages 2, 4 and 8. Kawai et al. compounds clearly anticipate the instant compounds/compositions of formula (I), wherein the variable M represents hydrogen or counter ion (i.e., Na), and the variable R represents alkyl, alkenyl or alkynyl.

Liliom et al. disclose a compound, see RN:182304-66-1, it clearly anticipate the instant compounds/compositions of formula (I), wherein the variable M represents hydrogen, and the variable R represents alkyl substituted with cycloalkane. Dependent claims 2 and 6-8 are also rejected along with claim 1 under 35 U.S.C. 102(b).

5.2 Claims 1-2, 4 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Mukai et al. US 2004/0214799.

Applicants claim compounds/compositions of formula (I) or (III), i.e.,



wherein the variable M represents

hydrogen or counter ion (i.e., Na), and the variable R represents alkyl, alkenyl or alkynyl, see claim 1 or 4.

Mukai et al. disclose a compound, i.e., compound No. 4 in Fig. 6, it clearly anticipate the instant compound of formula (III). Mukai et al. also disclose a number compounds, see compounds No. cPA-5, cPA-9, cPA-12, cPA-13, cPA-14, cPA-15, cPA-16, cPA-17, cPA-18, cPA-19, and cPA-20 in Fig. 2, and compound No. 6 in Fig. 6 (i.e., they are corresponding to compounds No. cPA-5, cPA-9, cPA-12, cPA-13, cPA-14, cPA-15, cPA-16, cPA-17, cPA-18, cPA-19, and cPA-20). Dependent claims 2 and 6-8 are also rejected along with claim 1 under 35 U.S.C. 102(b).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

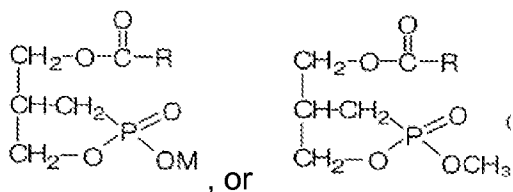
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6.1 Claims 1-3 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai et al. publication, Synthesis and Physiological Effects of Cyclic Lysophosphatidic Acid and Carba-Derivative, "The 23rd symposium on Progression Organic Reactions in Life Science," November 17 and 18 1997, The Pharmaceutical Society of Japan, pp. 1-9.

Applicants claim compounds/compositions of formula (I) or (II), i.e.,



, or wherein the variable M represents hydrogen or counter ion (i.e., Na), and the variable R represents alkyl, alkenyl or alkynyl, see claim 1 or 3.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kawai et al. disclose a number of compounds, i.e., PHYLPA, No. 6a-6f, and compounds No. 13a, 13c, 13d, and 13f, see pages 2, 4 and 8. Kawai et al. compounds

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Kawai et al. is that the Variable M represents hydrogen, counter ion or methyl, while Kawai et al. represents hydrogen, or counter ion. Kawai et al. compounds inherently overlap with the instant invention.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the instant claims 1-3 and 6-8 prima facie obvious **because** one would be motivated to employ the compounds of Kawai et al. to obtain the instant compounds/compositions of formula (I) or (II), wherein the variable M represents hydrogen, methyl (i.e., formula (II)) or counter ion (i.e., Na),

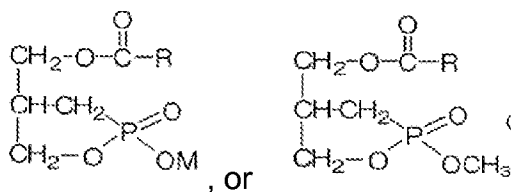
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and the variable R represents alkyl, alkenyl or alkynyl. It is well established that the substitution of methyl for hydrogen on a known Kawai et al. compound is not a patentable modification absent unexpected or unobvious results. *In re Wood*, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and *In re Lohr*, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). Dependent claims 2-3 and 6-8 are also rejected along with claim 1 under 35 U.S.C. 103(a).

The motivation to obtain the claimed methods of use derives from known Kawai et al. compounds would possess similar activity (i.e., pharmaceutical compositions) to that which is claimed in the reference.

6.2 Claims 1-3 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mukai et al. US 2004/0214799.

Applicants claim compounds/compositions of formula (I) or (II), i.e.,



wherein the variable M represents hydrogen or counter ion (i.e., Na), and the variable R represents alkyl, alkenyl or alkynyl, see claim 1 or 3.

Determination of the scope and content of the prior art (MPEP §2141.01)

$$\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_2\text{-O-C-R} \\ | \\ \text{CH-CH}_2 \\ | \\ \text{CH}_2\text{-O-P(=O)(OM)} \end{array}$$

, wherein the variable M represent hydrogen or a counter iron.

Determination of the difference between the prior art and the claims (MPEP

§2141.02)

The difference between the instant claims and Mukai et al. is that the Instant invention is compounds of formula (I) or (II), while Mukai et al. represents compounds of formula (I). Mukai et al. compounds inherently overlap with the instant invention.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the instant claims 1-3 and 6-8 prima facie obvious **because** one would be motivated to employ the compounds of Mukai et al. to obtain the instant compounds/compositions of formula (I) or (II), wherein the variable M represents hydrogen, counter ion (i.e., Na), or methyl (i.e., formula (II)) and the variable R represents alkyl, alkenyl or alkynyl. It is well established that the substitution of methyl for hydrogen on a known Mukai et al. compound is not a patentable modification absent unexpected or unobvious results. *In re Wood*, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and *In re Lohr*, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). Dependent claims 2-3 and 6-8 are also rejected along with claim 1 under 35 U.S.C. 103(a).

The motivation to obtain the claimed methods of use derives from known Mukai et al. compounds would possess similar activity (i.e., pharmaceutical compositions) to that which is claimed in the reference.

7. Claim 5 is neither anticipated nor rendered obvious over the art of record, and therefore are allowable.

Claim Objections

8. Claims 1-3 are objected to because of the following informalities: the term “may comprise”. Replacement of the term “may comprise” with the term “are optionally substituted with”, see claim 1, line 5.

9. Since claims 6-8 are drawn to a pharmaceutical composition, amendment of claims 6-8 as pharmaceutical compositions would obviate the objection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

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published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/REI-TSANG SHIAO /

Rei-tsang Shiao, Ph.D.
Primary Patent Examiner
Art Unit 1626

July 08, 2008